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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,757	07/28/2003	Yasuhiro Kouchi	Q76319	3310

23373 7590 01/13/2006

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EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 01/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/627,757	KOUCHI ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8, 10, 12-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,12 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-8 and 10 in the reply filed on 10/12/2005 is acknowledged. Claims 1-8, 10, and newly added claims 12-13 are pending and under consideration at this time. An action on the merits follows.

Claim Rejections - 35 USC § 112

2. Claims 1-8, 10, and 12-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method for predicting an increased risk for onset of any type of glaucoma based on the detection of any mutation in the coding region of any OPTN gene of any subject, wherein if any mutation is detected, the subject is predicted to have an increased risk for onset of any type of glaucoma. The claims are also further limited to any deletion, insertion or substitution in the coding region of an OPTN gene.

The claims are also drawn to a method for predicting an increased risk for onset of POAG or NTG or both, in any subject, by detecting any mutation in the coding region of an amplification product produced with an oligonucleotide primer pair consisting of nucleotide sequences "represented by" SEQ ID NOS 21 & 22; and 27 & 28, or a complement of such primers, or a primer which hybridizes to such primers, or a primer with 60% homology to such

primers. The claims are further limited to any OPTN gene which comprises nucleotides 1-1734 of SEQ ID NO: 1 (claims 2, 12) as well as to detection of one or both mutations A to G at position 619 or G to A at position 898 in SEQ ID NO: 1 (claims 3, 13).

While the claims encompass the coding region of "any" OPTN gene, no complete OPTN gene is taught by the specification. SEQ ID NO: 1 is drawn to the coding region of OPTN, and SEQ ID NOS: 2-14 appear to be drawn to exons 4-16 with partial intronic sequences. The specification does not teach OPTN sequences from any other species. However, claim 1 is drawn to any OPTN gene in any individual while claim 10 specifically encompasses a large genus of primers to variants and homologs of the single OPTN sequence taught in the specification. The recitation of primer pairs solely defined by the ability of each primer of the pair to hybridize to the primers in the pairs of SEQ ID NOS 21&22, or 27&28, or have 60% homology to each primer in the pair, and to optionally contain any substitution, deletion, insertion, or addition mutation, encompasses an extremely large genus of primers which would hybridize not only to variants and homologs of OPTN, but to completely unrelated sequences. The single OPTN sequence taught in the specification is not representative, structurally or functionally, of the number of possible variants, homologs, or unrelated sequences which could be associated with glaucoma. The claims encompass analysis of sequences that have not been taught or described by the specification, including sequences not known in the art at the time the invention was filed. For example, Accession number CAI16552, available after the filing date of the instant invention, teaches a protein sequence which differs from that predicted to be encoded by instant SEQ ID NO: 1.

Further, all of the current claims encompass a large genus of nucleic acids which comprise polymorphisms in the coding region of any OPTN gene, which are not disclosed in the specification. The genus includes an enormous number of polymorphisms and mutations for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named 2 polymorphisms for which data is provided. This data, however, does not provide for a predictable association with any type of glaucoma in any population, as is broadly claimed. Thus, applicant has express possession of only 2 particular polymorphisms in SEQ ID NO: 1, in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed which would permit selection of sequences as polymorphisms. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations of associating a polymorphism with risk of glaucoma onset is provided. Further, these claims expressly encompass all the different possible allelic variants including insertions, deletion, substitutions and transversions at thousands of different sites. However, no predictable correlation between the structural alterations of the 2 polymorphisms disclosed and a risk for glaucoma onset is provided by the specification. The specification does not teach the function of optineurin, nor how alterations are associated with glaucoma or an increased risk for glaucoma onset.

The specification provides no correlation between structure of polymorphisms and the function of such polymorphisms with an increased risk for glaucoma onset. The polymorphisms shown are not representative of the genus of any polymorphism associated with an increased risk for glaucoma onset because it is not clear which polymorphisms within the coding region of

"any" OTPN gene would have the same affect. The specification does not teach whether the polymorphisms shown affect the function of optineurin. The specification does not teach the function of optineurin nor how it's function, or lack of function, or altered function are predictably associated with glaucoma onset risk.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) In the instant case, the specification fails to teach the necessary common attributes or features of the genus of encompassed nucleic acids and polymorphisms in view of the species disclosed. As such, one of skill in the art would not recognize that applicant was in possession of the genus of nucleic acids and polymorphisms encompassed by the broadly claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic acids and polymorphisms, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. The current situation is a definition of the compound solely based on its functional utility, as a polymorphism, without any definition of the particular polymorphisms claimed.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

3. Claims 1-8, 10, and 12-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support

determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue. These factors have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and the breadth of the claims:

The claims are drawn to a method for predicting an increased risk for onset of any type of glaucoma based on the detection of any mutation in the coding region of any OPTN gene of any subject, wherein if any mutation is detected, the subject is predicted to have an increased risk for onset of any type of glaucoma. The claims are also further limited to any deletion, insertion or substitution in the coding region of an OPTN gene. The claims are further limited to POAG (primary open angle glaucoma) or normal ocular tension glaucoma (NTG). The claims are also drawn to a method for predicting an increased risk for onset of POAG or NTG or both, in any subject, by detecting any mutation in the coding region of an amplification product produced with an oligonucleotide primer pair consisting of nucleotide sequences "represented by" SEQ ID NOS 21 & 22; and 27 & 28, or a complement of such primers, or a primer which hybridizes to such primers, or a primer with 60% homology to such primers. The claims are further limited to any OPTN gene which comprises nucleotides 1-1734 of SEQ ID NO: 1 (claims 2, 12) as well as to detection of one or both mutations A to G at position 619 or G to A at position 898 in SEQ ID NO: 1 (claims 3, 13).

The nature of the claimed invention, therefore requires the knowledge of predictable associations between the presence of any mutation in any OPTN gene, or variant or homolog (claim 10) and increased risk of onset of any type of glaucoma in any human or non human subject.

The amount of direction or guidance and Presence and absence of working examples:

The specification teaches that blood from patients diagnosed as having open angle glaucoma were used to determine the sequence of the OPTN gene and compared to a non patient group (page 18). The specification teaches at page 15, that SEQ ID NOS: 21 and 22 were used to amplify exon 7 and SEQ ID NO: 27 and 28 were used to amplify exon 10. The specification teaches the identification of two mutations: A to G at position 619 and G to A at position 898 relative to SEQ ID NO: 1. The specification teaches that the frequency of the polymorphism at position 619 was 1.4 % in the patient group, and 0% in the non patient group, while the frequency of the polymorphism at position 898 was 0.8% in the patient group and 0% in the non patient group (page 19).

However, the specification is silent as to whether the frequency of the disclosed polymorphisms was statistically significant, as to how many patients and controls were tested, as to what the population origin of the patients and controls were (Caucasian, African, Japanese, Chinese, etc) and as to what type of open angle glaucoma the patients suffered from (primary adult onset: POAG or juvenile JOAG). The specification does not teach analysis with patients with normal tension glaucoma (NTG).

Further, the specification does not teach the function of the OPTN gene, or how the mutations detected affect the function of the OPTN gene, such that one of skill in the art could establish that a predictable correlation exists between the presence of any mutation in the coding region of OPTN and glaucoma in any subject. The specification does not teach mutations in an OPTN gene of any non human subject.

In light of the unpredictability taught in the art with regard to these factors, the specification does not enable one of skill in art to practice the method as broadly as it is claimed, without undue experimentation.

The state of the prior art and the predictability or unpredictability of the art:

At the time the invention was filed, the function of the optineurin was not known, and the art provided no predictable structure function correlation between any mutations in the coding region of OPTN and risk of onset of glaucoma. Rezaie (Rezaie et al; Science, vol. 295, pages 1077-1079, 2/2002) teaches that the function of OPTN is unknown. While Vittitow (Vittitow et al; Biochemical and Biophysical Research Communications, vol. 298, pages 67-74, 2002) teaches that expression of optineurin is increased in response to increased intraocular pressure (abstract), Kamphius (Kamphius et al; Ophthalmic Research, vol. 35, pages 93-96, 2003) teaches that optineurin gene expression level in the human trabecular meshwork was not changed in response to pressure elevation (see abstract).

Additionally, the post filing date art demonstrates the unpredictability of associating broadly "any" mutation in OPTN, with any type of glaucoma in different patient and non patient populations.

While Rezaie teaches that the R545Q mutation appears to be a disease causing mutation in Caucasian patients with adult onset POAG, Alward (Alward et al; Am. J. Ophthalmology, vol. 136, pages 904-910, 2003) teaches that it is likely to be a non disease causing polymorphism with marked ethnic differences in prevalence (see para bridging cols 1 and 2, page 109). Further, while Rezaie teaches that the M98K mutation appeared to be a risk associated alteration for NTG (table 1), Alward teaches that the M98K mutation was associated with a fraction of NTG only in patients with Japanese ethnicity but not in Caucasians (see abstract, col. 2, page 909). Leung (Leung et al; IOVS, September 2003, vol 44, pages 3880-3884), on the other hand, teaches that M98K and R545Q appear to be common polymorphisms in the normal Chinese population (page 3882, col 2). Alternatively, Tang (Tang et al; Human Genetics, vol. 113, pages 276-279; 2003) teaches that none of previously reported NTG risk mutations showed any significant differences among Japanese (see page 278, col. 1, "Discussion"). Further, Tang teaches that 10 out of 392 normal chromosomes contained the G to A mutation at position 1944 in the Japanese population, which differed from the 0 out of 100 chromosomes reported by Rezaie for Caucasians. Tang further exemplifies the need to provide large sample sizes for analysis. Wiggs (Wiggs et al; Arch. Ophthalmology. Vol. 121, 2003, pages 1181-1183) teaches analysis of mutations in exons 4 and 5, reported to be recurrent mutations in patients with NTG, in patients with adult onset POAG, and teaches that these mutations do not appear to be associated with adult onset POAG (see abstract).

The detection of new polymorphisms is an entirely unpredictable art which is empirical in nature, and once these polymorphisms are detected, their association with a phenotype, in this case, different types of glaucoma, must be established before they can be used in a predictive

manner. Even if an association is demonstrated between a single polymorphisms within a gene and a phenotype, it is not necessarily a predictor that a different polymorphism within the gene will also have the same predictive ability, as exemplified by the teachings in art cited above.

The level of skill in the art:

The level of skill in the art is deemed to be high.

The quantity of experimentation necessary:

In order to practice the invention as claimed, one would first have to establish that a predictive relationship exists between the disclosed polymorphisms and any type of glaucoma in any patient population. Given the lack of any information regarding sample size, patient and non patient populations, and statistical significance of the observed frequencies, such experimentation would be unpredictable as it cannot be established whether the observed frequencies were due to chance or would only be observed in such frequencies in a specific population, ie: Caucasian vs Chinese. The investigations set forth to support the instantly claimed invention are not independently replicated. In a technology that is known to be highly unpredictable, made more so by the lack of any structure function correlation between the disclosed polymorphisms and glaucoma, the lack of guidance with regard to sample size and population analysis is a particular cause for concern. Further, the scope of many of the claims requires knowledge of an association between all mutations in the coding region of any OPTN gene and any type of glaucoma in any human population or mammalian species, which as exemplified by the teachings in the art, is highly unpredictable. Due to the scope of the claims,

one would be required to further undertake extensive trial and error experimentation with a large number of patients with different types of glaucoma, and controls, including in different racial populations as well as other mammalian species, to determine mutations that share a predictive increased risk of glaucoma onset.

Therefore, in light of the breadth of the claims, the lack of guidance in the specification, the high level of unpredictability in the associated technology, the nature of the invention, and the quantity of unpredictable experimentation necessary to practice the claimed invention, it would require undue experimentation to practice the invention as claimed.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 10 and 12-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 recites in section 1, nucleotide sequences "represented" by 21, 22, 27, and 28. The recitation of "represented by" renders the claims indefinite because it is unclear if the term is meant to refer specifically to the sequences of SEQ ID NOS 21, 22, 27, and 28, or if the term is meant to refer to any sequence which is in some way related to SEQ ID NOS 21, 22, 27, or 28, for example, does a primer consisting of the sequence represented by SEQ ID NO: 21 refer to any sequences within the same region as SEQ ID NO: 21 or is it limited to the specific sequence of SEQ ID NO: 21? Additionally, the claims no longer recite the designation "SEQ ID NO:",

which should be placed before the recitation of 21, 22, 27, and 28 to make clear that such refers to a SEQ ID NO:.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1-2 and 4-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Sarfarazi (Sarfarazi et al, US Pregrant Publication 2004/0191798).

With regard to claim 1, Sarfarazi teaches and claims a method for predicting an increased risk for onset of glaucoma by assaying for the presence a mutation of at least one nucleotide of an OPTN gene of an individual , wherein when said mutation is present, said subject is predicted to have an increased risk for onset of glaucoma (see abstract, para. 0015, 0019, 0023, 0024). With regard to claim 2, Sarfarazi teaches a sequence comprising nucleotides 1-1734 of SEQ ID NO: 1 (SEQ ID NO: 1 taught by Sarfarazi). With regard to claims 4-6, Sarfarazi teaches detecting one or more insertions, deletions, or a change in one or more nucleotides (para 0023). With regard to claim 7, Sarfarazi teaches that glaucoma includes POAG and NPG (para 0016). With regard to claim 8, Sarfarazi teaches analysis using a probe that hybridizes to a coding portion (pages 4-6). See also claims 11-38 of Sarfarazi.

8. Claims 1, 2, 5, 7, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Rezaie (Rezaie et al; Science, vol. 295, pages 1077-1079, February 2002).

With regard to claim 1, Rezaie teaches a method of assaying for at least one nucleotide in the coding region of OPTN gene of a subject (see table 1, Figure 1, page 1078, col. 2-3). Rezaie teaches that 3 mutations were found: G458A; 691-692 insertion AG; G1944A (claims 2, 5) using either sequencing methods or SSCP (claim 8) to be disease causing mutations for adult onset POAG (claim 7), and that a fourth mutation, T603A (M98K), was a risk associated alteration. Rezaie teaches that individuals with this last mutation, who did not have glaucoma, could develop glaucoma in the future. The claimed recitation of "wherein said mutation is present, said subject is predicted to have an increased risk for onset of glaucoma" is considered an inherent property of the teachings of Rezaie given the statistically significant association for such mutations taught by Rezaie as well as the teaching that 3 mutations caused adult onset POAG and a fourth as a risk associated alteration.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claim 10 and ~~11~~ 12 92. are rejected under 35 U.S.C. 103(a) as being unpatentable over Sarfarazi in view of Genbank Accession number NT_031849 (February 2002)

With regard to claim 10, Sarfarazi teaches a method of diagnosing a risk of glaucoma in an individual by detecting an alteration at codon 322, which is in exon 10, (claims 29-32). Sarfarazi teaches that analysis of mutations can involve amplification of a portion of the optineurin gene comprising the alteration, such as a portion containing at least one exon (see para 0027). Sarfarazi does not teach utilizing primers with the sequence of instant SEQ ID NOS 27 and 28, however it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, in view of the teachings of the genomic sequence of OPTN taught by Genbank Accession number NT_031849, to construct a genus of primer pairs for amplification of exons containing mutations as taught by Sarfarazi, including primers that would amplify exon 10 which contains a mutation at codon 322, as taught by Sarfarazi. Such genus of primers is considered functionally equivalent to the claimed primer pair and genus of primer pairs as listed in instant claim 10, absent secondary considerations, and are obvious over the teachings of Sarfarazi in view of Genbank Accession number NT_031849. The ordinary artisan would have been motivated to construct such primer pairs because Sarfarazi teaches to detect the

presence of such mutations in individuals and further teaches that analysis encompasses amplification of an exon with the mutation.

Conclusion

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jehanne Sitton

Jehanne Sitton
Primary Examiner
Art Unit 1634
1/9/06